PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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PCT

WRITTEN OPINION
(PCT Rule 66)

Date of mailing *(day/month/year)*	08.03.2004
Applicant's or agent's file reference: 2948-177.PCT	**REPLY DUE** **within 3 month(s)** from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US 03/21061	07.07.2003	08.07.2002

International Patent Classification (IPC) or both national classification and IPC
A23L3/3571

Applicant
EXPONENTIAL BIOTHERAPIES, INC. et al.

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☒	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain documents cited
VII	☐	Certain defects in the international application
VIII	☐	Certain observations on the international application

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3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4. For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis. For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 08.11.2004

Name and mailing address of the international preliminary examining authority:

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I. Basis of the opinion

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed")*:

Description, Pages

1-18 as originally filed

Claims, Numbers

1-48 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

5. ☐ This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

☐ the entire international application,

☒ claims Nos. 20,21

because:

☒ the said international application, or the said claims Nos. 20,21 relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

2. A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequence listing to comply with the Standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1, 4-15, 35-46
Inventive step (IS)	Claims	1,4-15, 35-46
Industrial applicability (IA)	Claims	

2. Citations and explanations

see separate sheet

Re Item III
Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

For the assessment of the present claims 20 and 21 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Re Item V
Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: Applied and Environmental Microbiology (1993), 59(9), 2914-2917
D2: Applied and Environmental Microbiology (07-2000), 66(7), 2951-2958
D3: DE-C-4326617
D4: Applied and Environmental Microbiology, Washington,DC, US (01-04-1996), 62(4), 1133-1140
D5: GB-A-2253859

Observations:

Claims 20 and 21 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

1. Novelty - Article 33(1) and (2) PCT

The subject-matter of independent claim 1 is not novel for the following reasons:
D1 is considered to anticipate all the essential features of claim 1. The argument that

the phages described in D1 are not "virulent" but temperate (see also description pages 2 and 3) of the present application cannot be accepted for the following reasons:
The so-called "temperate" phages, used in D1 also induce lysis of *Listeria monocytogenes* , which indicates that the phages of D1 are used in their "virulent" state.
More important, the entire expression "wherein said phage is virulent against a particular serovar" is unclear (Art. 6 PCT) and attempts to define the subject-matter of claim 1 in terms of the result to be achieved, which merely amounts to a statement of the underlying problem, i.e. finding suitable phages for a particular serovar. Consequently, this expression is not taken into consideration for assessing novelty.
Similar observations apply in view of D5. Using bacteriophages for controlling *Listeria sp.* in foodstuffs is known from the prior art. Specifying which serovar you want to control is defining the problem in a more detailed way and this does not add any novel feature to the subject-matter of said claim.

D3 discloses the virulent phage (myovirus) A511 and states (column 1, paragraph 4 - column 2, paragraph 1) that the phages comprising the endolysins but also the purified endolysins are lytic for *Listeria monocytogenes* and can be used for controlling contamination in foodstuffs.
D4 discloses a method of detecting *Listeria* in foodstuffs (= controlling *Listeria* contamination) by applying the A511 phage to contaminated food. Implicitly, the amount of *Listeria* will be reduced to some extent due to lysis caused by the bacteriophages. Since claim 1 does not contain features which distinguish its subject- matter clearly from the disclosure of D4, said claim is not novel in view of D4.

The feature "phage P100" is novel in view of the documents of the search report.

2. Inventive Step - Article 33(1) and (3) PCT

The question whether the application involves an inventive step is only of relevance once novelty of the independent claims has been established.
It is suggested to incorporate the subject-matter of claim 2 in all independent claims.
It is considered that the specific endolysin produced by phage P100 can only be obtained from the P100 phage (see also description page 8, lines 12-15). Since the endolysin protein has not been characterized in any other way claims 35 and 43 should be reworded in order to indicate that the endolysin is derived from phage P100. Claim

39 should be deleted since its subject-matter is vague and unclear (Art. 6 PCT).

3. The following observations are also made:

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D2-D5 is not mentioned in the description, nor are these documents identified therein.

The number of independent claims should be reduced (Art. 6 PCT).